Appln No.: 10/646,391
Amendment Dated: July 8, 2005
Reply to Office Action of April 8, 2005

REMARKS/ARGUMENTS

This is in response to the Office Action mailed April 8, 2005 for the above-captioned application. Reconsideration is respectfully requested.

Claim 5 has been amended to delete the extra parenthesis in view of the Examiner's remarks.

The Examiner maintained the restriction requirement, and objected to claim 3 as reading on non-elected subject matter. Applicants submit that claim 3 is generic with respect to the elected invention. The Examiner further objects to claims 6 and 9 which names Seq ID Nos including the elected Seq ID No. as duplicates of other claims. Again, these claims are generic and encompass the elected sequence as well as other species joined by the linking generic claims. The reason for the objection to these claims is unclear as is the nature of the response the Examiner might be looking for. If the linking generic claim 1 is found to be allowable, then claims 3, 6 and 9 should also be allowed in this application, without amendment.

The Examiner rejected claims 1-10 under 35 USC § 112, first paragraph, as lacking enablement. Applicants respectfully traverse this rejection.

The Examiner asserts that the disclosure of activity of antisense sequences against clusterin in human melanoma cell lines *in vitro* and the general teaching as to the methods of employing this antisense in the treatment of melanoma is not sufficient to enable the methods of the invention. In support of this, the Examiner does not specifically statement why undue experimentation would be required in the context of the present invention, but instead cites various references about general unpredictability associated with antisense technology. Applicants submit that this is insufficient.

The Examiner cites Branch for a teaching that not all complementary oligonucleotides are effective as antisense. However, Applicants disclose specific human antisense species that have been shown to have antisense activity and show this activity in human melanoma cells. The Green paper is dated from 2000, and therefore must be considered old in this rapidly developing technology. Further, it refers to problems such as toxicity which are not of concern in determining enablement since all that is required for enablement is some level of efficacy.

The Jens article, also dated in 2000 and therefore old with respect to the technology, describes problems with delivery of antisense *in vivo*. However, test results using clusterin antisense in connection with other clusterin-expressing tumors have shown that there are no special needs for delivery of the antisense. A copy of a declaration submitted in a related case (09/967,726) showing *in vivo* testing in humans using intravenous administration is attached.

Although the study was intended to toxicity, the antisense arrived at and was effective to bring about clinical improvements in prostate and ovarian cancer patients. Nothing in Jens suggests that for this type of antisense this would not also be the case with melanoma which is shown in the present application to express clusterin.

In view of the foregoing, Applicants submit that the Examiner has not met the burden of establishing undue experimentation to practice the method of the invention. Determination of pharmacokinetics and appropriate dosing levels is routine, and the use of anti-clusterin antisense poses no special challenges.

The Examiner rejected claims 1-5 under 35 USC § 102(a) as anticipated by Monia et al., US 2004/0053874). As a first matter, Applicants point out that the appropriate citation in this instance is to 102(e), since Monia was published after this application was filed. The Examiner states that Monia is anticipatory because it teaches treating a disease or condition associated with clusterin expression by administration of a compound that inhibits expression of clusterin. Applicants assume that the Examiner is relying on Applicants' disclosure that clusterin is expressed in melanoma cells since Monia does not mention melanoma. This is improper. To be anticipatory, the reference must disclose applicants' invention, and Monia does not teach that targeting clusterin expression would be appropriate for the treatment of a melanoma. Thus, the rejection should be withdrawn.

The Examiner rejected claims 1-5, 9 and 10 under 35 USC § 102(B) as anticipated by Gleave et al., WO 00/49937. This reference discloses antisense therapeutic that target clusterin expression but does not mention their use in the treament of melanoma. Accordingly, this reference does not teach the claimed invention and is not anticipatory.

The Examiner rejected claims 1-5, 9 and 10 under 35 USC § 102(a) as anticipated by Gleave (US 2002/0128220) This reference discloses antisense therapeutic that target clusterin expression but does not mention their use in the treament of melanoma. Accordingly, this reference does not teach the claimed invention and is not anticipatory.

The Examiner rejected claims 1-10 under 35 USC § 103(a) as unpatentable over Gleave et al., WO 00/49937 in view of Baracchini (US 5,801,154). Baracchini is cited only with respect to backbone modifications, and does not overcome the fact that Gleave says nothing about treatment of melanoma. Accordingly, the combination of references does not suggest the claimed invention which is a method for treating melanoma. The rejection should therefore be withdrawn.

Finally, the Examiner has provisionally rejected claims 1, 2, 9 and 10 for obviousness type double patenting over claims 1-3 of copending application 10/828,394. The '394

application claims treatment of cancerous angiogenesis related disease using materials that inhibit clusterin expression. The present claims are directed to treatment of melanoma using the same type of materials. The Examiner has not established that melanoma is a cancerous angiogenesis related disease, and melanoma is not mentioned in the '394 application. Accordingly, the Examiner has not established that there is any overlap in the claimed subject matter that would make a double-patenting rejection appropriate. Furthermore, claims in the '394 application have not been allowed, so it is not clear whether a terminal disclaimer would be ultimately appropriate.

Applicants are concurrently filing a Supplemental Information Disclosure Statement. Because of the number of references, this paper is being filed by mail. Consideration of the references listed thereon prior to the issuance of the next paper in this case is requested.

Respectfully submitted,

Marina T. Larson Ph.D.
PTO Reg. No. 32,038
Attorney for Applicant
(970) 468-6600

Attachment:

copy of declaration from 09/967,726.